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Original Article

Study of Smoking Pattern and Cognitive Changes in Chronic Obstructive Pulmonary Disease Patients Attending Tertiary Care Center in Kerala

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Abstract

Cognitive dysfunction is an important systemic effect of COPD affecting various cognitive domains. The mechanisms involved in the impairment of cognition and the relevant factors are complex and not fully understood. Our study aimed at evaluating the cognitive function in relation to different parameters of smoking in patients with established COPD. In a hospital based cross sectional study, we examined hundred consecutive COPD patients for cognitive skills of orientation, attention, memory, visuo perceptual abilities and executive functions by neuropsychological battery of tests. Impact of smoking pattern on each cognitive skill was examined by grouping these patients based on several dimensions of smoking. It was found that with the age of commencement of smoking ie; those who started smoking early in life had impairment in orientation than those who started late ($p<0.05$). And those patients who smoked both cigarette and beedi performed poor with CDT and took more time to complete the task TMT-A, which was statistically significant at $p<0.05$. We also found that COPD patients categorised as severe smokers and those with maximum duration of smoking (>20 yrs) performed poorly with CDT which was statistically significant at $p<0.05$. Thus, we could find a noticeable impact of smoking pattern on cognitive function. Among the various cognitive domains, visuospatial impairment, constructional praxis, and impairment of cognitive flexibility, visual search, motor performance, and executive function were the most affected.

Introduction

The World Health Organization (2009) estimates that about 210 million people worldwide have COPD (1). The twentieth century spread of tobacco use led to a global epidemic of smoking-related illnesses, resulting in 5.4 million deaths worldwide each year. The yearly toll is expected to surpass 6 million by 2015. By then, approximately 30% of the tobacco-related deaths will be caused by chronic respiratory diseases (1). Cigarette smoking is the leading cause of chronic obstructive pulmonary disease (COPD). The risk of COPD is 56-fold higher in current smokers than in never-smokers (2). Passive exposure to smoking, air pollution, and occupational chemical fumes or dust may act synergistically with active smoking to increase the risk of COPD (3).

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COPD is defined as a disease characterized by progressive, irreversible airflow limitation and abnormal inflammatory response in the lungs (4). A recent review article indicates cognitive impairment in patients with COPD (5). This suggests that COPD is associated with specific abnormalities in brain structure.

Cognitive functioning can be divided into several cognitive domains, such as information processing, attention and concentration, memory, executive functioning, and self-control (6). A review by Durazzo et al. found poorer domain-specific cognitive skills, including auditory-verbal learning and memory, information processing speed, cognitive flexibility, executive functions, general intelligence, reasoning, sustained attention and impulse control, visual search speeds, and working memory among smokers, compared to non smokers (7).

Because smoking is a primary risk factor for COPD and other lung disorders, smoking may have an indirect effect on cognitive functioning through its impact on lung function (8). Previous studies could not demonstrate a precise pattern of cognitive impairment in COPD patients. However, some studies have shown an association between lung function and cognitive function, regardless of smoking status (5). Our objective was to assess the effect of pattern of smoking on cognitive function using a multiparametric assessment.

Methods

A cross sectional study was conducted among (n=100) consecutive subjects currently non smokers, aged >40yrs with COPD as defined in the Global Initiative for obstructive lung disease (GOLD-2014) guidelines (9), attending for review in outpatient unit of department of the Respiratory medicine in Govt. T D Medical College Hospital, Alappuzha during January 2015 to July 2015. They were treated only with necessary medications for COPD. The purpose of the study was explained to the patients and explicit written consent was obtained thereof. Institutional ethical clearance was obtained for the study by institutional review board of Govt. T.D.M.C. Alappuzha.

Inclusion criteria for the study are- Selection of COPD patients aged >40 yrs, as per the GOLD guidelines and patients with at least high school education, as low educational levels substantially increase the likelihood of misclassifying normal subjects as cognitively impaired (10).

Exclusion criteria -Patients with neurological disorders, history of depression (Hamilton depression rating scale HAM-D-21 > 8, not included in the study (11), Patients on continuous oxygen therapy, or with other comorbidities like, hypertension, diabetes mellitus, previous stroke, tuberculosis, pneumonia or carcinoma lung**,** anaemia, electrolyte imbalances and patients with visual or hearing impairment.

Spirometry-All the patients were performed post-bronchodilator spirometry (*spiropalm 6MWT comply with ATS/ERS guidelines*) and those with FEV_1 less than 80% of the predicted value along with an FEV_1/FVC % not more than 70% were included in the study.

Neuro-psychological evaluation-Cognitive function was evaluated using four vali-dated psychometric questionnaires: 1) the Mini Mental Status test (MMSE) (12), which assesses spatial and time orientation, attention, and calculation (education with at least eight grade (10); Normal score: ≥27 points; moderate cognitive impairment: 24–18 points; severe cognitive impairment: <18 points); In present study, MMSE was administered in their native language [Malayalam] by exact conversion of the questions of MMSE International Version in English. 2) the Clock Drawing test, which assesses memory, attention, and symbolic representation A score of e”3 represents a cognitive deficit, while a score of 1 or 2 is considered normal (13). 3) The Trail Making test TMT-A (14), which assesses visual processing and reproduction of numeric sequences (cognitive impairment: ≥94 seconds); and 4) the TMT- B (15), which assesses cognition flexibility and shifting capacity (cognitive impairment: ≥283 seconds).

Smoking- Data on cigarette smoking were collected using questions on smoking status, age at which the participant started smoking (<20 yrs, 20-30 yrs and >30 yrs), type of smoking (cigarettes, bidi or

both), average number of cigarettes/beedi per day (smokers with less than 10 as mild, 10-19 as moderate, and 20 or more as severe smokers). Duration of smoking (<11 yrs, 11-20 yrs and >20 yrs), Years since stopped (<5 yrs, ≥5 yrs), Age at which the patient started smoking.

Statistical analysis

Statistical analysis was done using SPSS version 18, statistical software (SPSS, Inc., Chicago, USA). One way Analysis of variance (ANOVA) was used to compare mean test scores of cognitive tests among the COPD patients with respect to smoking parameters (P<0.05 indicated statistical significance).

Result

When different patterns of smoking were assessed with the neuropsychometric scores (Table-I) There was a significant difference noted with the age of commencement of smoking and orientation (p<0.05). We could not find any significant changes with type of smoking, cigarettes/bidi smoked per day, and years since stopped with cognitive scores. We noticed a trend with the duration of smoking that patients with less duration of smoking gave a better result with orientation, registration and attention, but not statistically significant.

From Table-II, we observed that, those patients who smoked both cigarette and bidi performed poor with CDT and took more time to complete the task TMT-A, which was statistically significant at p<0.05. We also found that COPD patients categorised as severe smokers and those with maximum duration of smoking (>20 yrs) performed poorly with CDT which was statistically significant at p<0.05. There was

TABLE I: Effect of smoking on cognitive domains in COPD.

Category (max score)	*N*	*Orentation (10)*	*Registration (3)*	*Attention (5)*	*Recall (3)*	*Language verbal (8)*	*Copying (1)*
Type of smoking		Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
bidi	34	9.00±1.954	2.88±0.327	3.56±1.521	2.15±0.784	7.29±0.938	0.09±0.288
cigarette	19	8.58±2.219	2.74±0.806	3.00±1.247	1.95±0.848	7.21±0.918	0.00±0.000
both	6	9.00±1.549	3.00±0.000	3.50±1.378	2.17±0.753	6.83±0.408	0.00±0.000
P Value		0.755	0.472	0.388	0.664	0.513	0.325
Cigarettes/Day	N	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
<10 (Mild)	18	9.22±1.478	2.67±0.840	3.44±1.580	2.22±0.878	7.50±0.707	0.06±0.236
10-19- (Moderate)	17	9.18±1.811	2.94±0.243	3.53±1.328	2.00±0.791	7.18±0.883	0.00±0.000
≥20 (Severe)	24	8.38±2.374	2.92±0.282	3.21±1.414	2.04±0.751	7.04±0.999	0.08±0.282
P value		0.297	0.208	0.758	0.677	0.254	0.500
Duration of smoking (years)	N	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
<11	7	10.00±0.000	3.00±0.000	4.14±1.215	2.14±0.900	7.57±0.535	0.14±0.378
11-20	6	9.17±0.983	2.83±0.408	3.33±1.366	2.17±0.753	7.17±0.983	0.00±0.000
>20	46	8.65±2.173	2.83±0.570	3.26±1.452	2.07±0.800	7.17±0.926	0.04±0.206
P value		0.232	0.716	0.317	0.939	0.548	0.463
Years since stopped	N	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
<5	26	9.04±1.928	2.81±0.491	3.54±1.334	2.19±0.801	7.35±0.936	0.04±0.196
>=5	33	8.73±2.050	2.88±0.545	3.24±1.501	2.00±0.791	7.12±0.857	0.06±0.242
P value		0.585	0.606	0.433	0.360	0.341	0.707
Age at onset (years)	N	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
<20	8	7.25±1.753	3.00±0.000	3.62±1.061	2.25±0.707	7.38±0.916	0.00±0.000
20-30	18	7.89±2.698	2.78±0.732	3.06±1.662	2.00±0.907	7.06±0.938	0.11±0.323
>30	33	9.30±1.357	2.85±0.442	3.48±1.372	2.09±0.765	7.27±0.876	0.03±0.174
		0.04*	0.610	0.518	0.765	0.624	0.368

Values are expressed as Means±SD; ANOVA, Analysis of variance .*Significant at P<0.05 level.

TABLE II: Variation of neuropsychometric scores with smoking categories in COPD.

Category *Normal reference value*		*MMSE* *>24*	*CDT* *<3*	*TMT-A* *<94 sec*	*TMT-B* *<283 sec*
Type of smoking	N	Mean±SD	Mean±SD	Mean±SD	Mean±SD
bidi	34	24.97±4.502	3.47±1.562	126.106±82.985	113.62±130.575
cigarette	19	23.47±4.858	3.89±1.560	120.632±81.341	68.95±110.580
both	6	24.50±2.074	5.17±0.983	274.167±103.802	37.33±91.448
P value		0.508	0.046*	0.001*	0.234
Cigarettes/Day	N	Mean±SD	Mean±SD	Mean±SD	Mean±SD
<10 -Mild	18	25.11±4.484	3.94±1.731	112.733±88.898	89.73±105.49
10-19- Moderate	17	24.82±3.678	3.00±1.414	146.280±80.469	119.00±151.430
>=20- severe	24	23.67±4.931	4.21±1.414	150.333±109.097	69.62±104.323
P value		0.539	0.04*	0.455	0.418
Duration of smoking (years)	N	Mean±SD	Mean±SD	Mean±SD	Mean±SD
<11	7	27.00±2.160	2.86±1.069	126.571±75.119	174.14±112.600
11-20	6	24.67±3.670	2.67±2.251	135.450±80.240	133.88±158.610
>20	46	24.02±4.697	4.07±1.451	142.159±101.313	70.61±111.535
P value		0.256	0.029*	0.917	0.064
Years since stopped	N	Mean±SD	Mean±SD	Mean±SD	Mean±SD
<5	26	24.96±4.512	4.04±1.509	132.385±85.734	70.85±109.504
>=5	33	24.03±4.405	3.58±1.621	144.927±102.447	107.73±130.970
P value		0.428	0.267	0.618	0.254
Age at onset (years)	N	Mean±SD	Mean±SD	Mean±SD	Mean±SD
<20	8	25.50±3.586	3.12±1.126	164.50±134.264	74.88±80.446
20-30	18	22.89±5.666	4.17±1.465	134.57±99.545	58.89±89.803
>30	33	25.03±3.721	3.73±1.701	135.98±82.597	114.97±143.456
P value		0.200	0.291	0.729	0.267

Values are expressed as Means±SD; ANOVA; Analysis of variance. *Significant at P<0.05 level Abbreviations - MMSE, Mini Mental Status test; CDT, clock drawing test; TMT A, Trail Making test A; TMT B, Trail Making test B.

also an increasing trend of poor performance with TMT-A as the amount and duration of smoking increased, but not statistically significant.

We did not find any significant change in cognitive scores of COPD patients with the duration of quitting smoking and age at which the smoking started. Also we did not notice any change with MMSE and TMT-B scores with any of the smoker category.

Discussion

Neuropsychological tests aim to provide standardised and objective measurement of the functioning of one or more specific cognitive domains. Performance within each domain depends on one or more of the main classes of cognitive function (16). We used a multi parametric psychometric measures that are able to inform on several domains of cognition. We have already hypothesized in our earlier study that there was a significant decline in the cognitive function in COPD patients when compared to the normal healthy individuals (17). In the present study we focussed on the association of various patterns of smoking on cognition, as among the several risk factors, Cigarette smoking is considered as the leading cause of chronic obstructive pulmonary disease (COPD)(2).

Our study elucidated quantity of cigarettes/bidi smoked per day, type of smoking and duration of smoking had more risk in cognitive impairment. In this study the adverse impact of smoking was greater on executive function, visuospatial functions, constructional praxis, cognitive flexibility, visual

search and motor performance. We also observed that orientation was affected in patients who started smoking early in life. A different study by Jacobsen and colleagues observed greater impairment in working memory performance accuracy in adolescents who began smoking at younger age than those who began smoking at older age (18). In previous study impairment in specific cognitive domains was found to be positively related to the level of chronicity of smoking (19). These findings implicate a continuum of toxicity, whereby earlier exposure to nicotine is associated with greater brain damage than is exposure occurring at later age. Several longitudinal studies have found associations with middle-age smoking and cognitive dysfunction in males over a 20-yr period (20). A multicentre European cohort showed that yearly decline in MMSE was associated with smoking status (21). A different study has showed that cognitive deficits associated with smoking include reduced processing speed, verbal memory and MMSE (8). Thus, Cognitive impairment in these patients can be attributed to the deleterious effects of nicotine.

There are various mechanisms that explain cognitive impairment related to smoking. One mechanism is smoking may promote cerebral atherosclerosis and exacerbate cerebral hypoxia due to chronically elevated carbon monoxide causing a left shift of the oxyhaemglobin dissociation curve (22). It may also affect the microstructural integrity of cerebral white matter due to the stimulating effect of nicotine on nicotine receptors and induction of cerebral small-vessel disease (23), affecting cognitive function. Certain particles in cigarette smoke are thought to have a direct neurotoxic effect with heavy metal constituents of smoke being linked to an increased risk of Alzheimer's disease (24-25).

Another mechanism that could underlie the association between smoking and cognitive decline is lung function (26). Smoking is a risk factor for lung injuries that can increase risk of cognitive impairment and dementia (27-28). However, we have already hypothesized the association between lung function and cognitive decline in our previous study (29).

Also, some studies have found associations between impaired lung function and cognition that is independent of current and lifetime smoking status (30).

Thus, Cognitive impairment in COPD being multifactorial, it is necessary to study each factor, adjusting the other factors to assess the direct association of these with cognitive status.

In conclusion, cognition can deteriorate substantially in subjects with chronic airway flow limitation i.e., COPD. Smoking, being one of the leading causes of COPD, can affect cognitive impairment either directly through toxic substances present in it or indirectly by impairing the lung function. Our study clearly shows that among the various pattern of smoking the type and quantity of cigarettes/bidi smoked/day, duration of smoking and the age at onset of smoking, had more impact on cognition especially on orientation, visuospatial impairment, constructional praxis, and impairment of cognitive flexibility, visual search, motor performance, and executive function.

Implication of the study- Smoking is one of the leading global problems, health education should be imparted in various educational institutions and health care centres regarding the deleterious effects of smoking. Smoking cessation should also be a part of the management of patients with COPD complicated by cognitive dysfunction. Health workers can arrange resources like assistance from a social network and environmental structure in order to enhance the success in quitting smoking.

Conflicts of interest

The authors report no conflicts of interest in this work.

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